Colledge, S., Leung, J., Larney, S., Peacock, A., Grebely, J., Hickman, M., Cunningham, E., Trickey, A., Stone, J., Vickerman, P., & Degenhardt, L. (2020). Frequency of injecting among people who inject drugs: A systematic review and meta-analysis. *International Journal of Drug Policy*, *76*, [102619]. https://doi.org/10.1016/j.drugpo.2019.102619

Frequency of injecting among people who inject drugs: a systematic review and meta-analysis

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Word count: 4336

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Abstract

Background: People who inject drugs (PWID) do so at varying frequencies. More frequent injecting is associated with skin and soft tissue infection, blood borne viruses, and overdose. The aims of this review are to estimate the prevalence of injecting frequency among PWID and compare these estimates to current needle-syringe distribution coverage estimates, and identify socio-demographic and risk characteristics, and harms associated with daily or more injecting.

Methods: We conducted a systematic review of the peer-reviewed and grey literature from 2008 to 2018 and extracted needle-syringe distribution coverage data from a recent systematic review. We generated country-, region-, and global-level estimates of daily or more injecting. We also ran meta-regression analyses to determine associations between daily or more injecting and socio-demographic characteristics, injecting risk behaviour, non-fatal overdose, injection site skin infection, and blood borne virus prevalence.

Results: Our search resulted in 61,077 sources, from which 198 studies were eligible for inclusion in this review. There were 74 countries with estimates for injecting frequency. Globally, we estimated that 68.1% (95%CI 64.5, 71.6%) of PWID, equating to approximately 10.5 (95% UI 6.8-15.0) million people, inject daily or more frequently. There was a higher percentage of participants reporting daily or more injecting among samples with shorter injecting careers, more male participants and higher reporting of opioids as their main drug injected. Daily or more injecting was also associated with samples reporting a higher prevalence of HIV and hepatitis C antibody (anti-HCV), non-fatal overdose, and receptive needle sharing in the previous month.

Implications: WHO recently recommended a needle-syringe distribution target of 300 needles per PWID per year which is unlikely to be sufficient for the majority of PWID injecting daily or more who are out of drug treatment.

Funding: The Australian National Drug and Alcohol Research Centre, Australian National Health and Medical Research Council, University of New South Wales

Keywords: injecting drug use, people who inject drugs, population size, injecting behaviour, needle and syringe programmes, harm reduction, needle-syringe distribution coverage

Introduction

Globally, there are an estimated 15.6 million people who inject drugs (PWID) (Degenhardt et al., 2017). People who inject do so at varying frequencies. More frequent injecting has been associated with higher-risk injecting practices such as re-using and sharing injecting equipment and injecting into the neck and femoral vein (Darke, Swift, Hall, & Ross, 1994; Rafful et al., 2015; Tarján et al., 2015; Wilson, Brener, Mao, & Treloar, 2014), which also increases risk of severe harms such as blood borne viral infections and thrombophlebitis (Corneil et al., 2006; Miller et al., 2006; Rafful et al., 2015; Schoenbaum et al., 1989; Todd et al., 2011). More frequent injecting is also independently associated with several health harms including injection site skin infection and overdose (Blackburn et al., 2017; Brugal et al., 2002; Kinner et al., 2012; Lafferty, Smith, Coull, & Shanley, 2016; Larney, Peacock, Mathers, Hickman, & Degenhardt, 2017; Noroozi et al., 2018; Robinson et al., 2017).

Multiple factors may contribute to the variation in injecting frequency. For example, PWID with longer injecting careers who have an increased tolerance, or are transitioning from experimental drug use to dependence, may be injecting higher doses but also more frequently (National Institute on Drug Abuse, 2007). Similarly, drug type can mediate injecting behaviour; relative to an opiate, cocaine has a short half-life (approximately 30 minutes) and therefore injecting may occur more frequently in order to sustain a high (Korsmeyer & Kranzler, 2009; van Beek, Dwyer, & Malcol, 2001). In contrast, PWID in opioid agonist treatment (OAT) typically inject less frequently than those out of treatment (Mattick, Breen, Kimber, & Davoli, 2009; Platt et al., 2018; Scott, Caulkins, Ritter, & Dietze, 2015). As well as individual factors, local societal factors can also contribute to variation in injecting frequency. These might include drug market characteristics and drug policy that govern the availability of different drug types and the provision of drug treatment and other harm reduction services (Day, Degenhardt, Gilmour, & Hall, 2004; MacArthur et al., 2012).

Measuring injecting frequency is important for informing harm reduction services, such as needle and syringe programs (NSPs). NSPs distribute sterile injecting equipment to PWID and are an important part of the global response to reduce the transmission of blood borne viruses. The World Health Organization (WHO) (2016) recently suggested a target of 300 needles distributed per PWID per year

to improve coverage and reduce the transmission of blood borne virus infection; however, this target assumes less than daily frequency of injecting for PWID. Identifying frequency of injecting across countries is critical to understand sufficiency of this target distribution, yet to our knowledge there has been no systematic review of frequency of injecting by country and globally. Therefore, we aimed to:

- Estimate country, regional, and global-level injecting frequency among PWID;
- Identify socio-demographic and injecting characteristics associated with frequency of injecting among PWID;
- Evaluate the associations between frequency of injecting and engaging in injecting risk behaviour, non-fatal overdose, HIV prevalence, hepatitis C antibody (anti-HCV) prevalence and recent skin and soft tissue infection; and
- Compare country-level injecting frequency estimates to country-level NSP coverage.

Methods

Data source

Data for this review comes from a broader systematic review investigating prevalence of injecting, socio-demographic and risk characteristics of PWID (defined henceforth as people who have injected drugs within the previous year), and blood borne virus prevalence among PWID globally (Degenhardt et al., 2017). The review protocol is registered with PROSPERO (record number CRD42016052853) and reported according to PRISMA (Moher, Liberati, Tetzlaff, Altman, and The (2009); Appendix 1) and GATHER guidelines (Stevens et al. (2016); Appendix 2). In 2016, peer-reviewed literature (Medline, Embase, and PsycINFO), grey literature and online databases were systematically searched, and data requests were sent to international experts and agencies for literature published from 2008 onwards. Peer-reviewed literature searches were updated in June 2017 and July 2018. We searched for sources with estimates of injecting drug use (IDU) prevalence, characteristics of PWID including socio-demographic and risk characteristics, frequency of injecting, injecting-related injuries and diseases, and serologically confirmed blood borne virus prevalence. Search terms included keywords with explosions of terms for IDU and epidemiology, IDU and HIV, and IDU and infections (Appendix 3 and 4).

Screening and study selection

Two researchers independently screened studies for inclusion, and all conflicts were resolved in discussion or consultation with a third researcher. Data were extracted into a Microsoft Access Database, and exported and cleaned in Microsoft Excel. Where there were multiple studies reporting on the same sample, the study with the most complete information was included. In the current review, studies with data on frequency of injecting by PWID (self-report) were included, unless: a) there were fewer than 40 (PWID) participants in the sample, b) the sample was a subpopulation (e.g. samples of PWID who were HIV-positive or incarcerated), c) the inclusion criteria specified daily (or more frequent) injecting, d) the most frequent category for injecting was monthly or more (or less frequent), e) the study was an earlier iteration of a more recent study, or f) there was an age restriction on the sample (i.e. other than restricting to adult PWID).

Measures

Frequency of injecting was extracted as categorised in the source and then coded to our definitions to create consistency across studies (the definitions are provided in Appendix 5). We originally intended on presenting the data in the detailed categories defined in Appendix 5; however, frequency categories and definitions varied greatly between studies. These broader definitions were therefore combined to create binary 'daily or more' and 'less than daily' estimates for each study. We based our definitions on the most commonly reported injecting frequency categories. Several studies did not conform to our definitions of injecting frequency, and our decision process for including studies in our analyses is reported in Appendix 6.

There were nine study-level exposure variables that we aimed to investigate: year of data collection; median (or mean if median was not reported) duration of injecting (in years); and self-report proportion of the sample that were female, young (defined as ≤25 years), reported current engagement in opioid agonist treatment (OAT), opioids as their main drug injected, stimulants as their main drug injected, unstable housing or homelessness within the previous 12 months, and incarceration within the previous 12 months. Region and country-level income class (low, lower-middle, upper-middle, and high) (World Bank, 2018) were also extracted into the dataset.

Considering frequency of injecting as the predictor variable, there were also five outcome variables we aimed to investigate: the proportion of participants engaging in recent risky injecting behaviour (defined as receptive needle or syringe sharing in the previous month); serologically confirmed HIV and anti-HCV prevalence; self-reported non-fatal overdose in the previous 12 months; and self-reported skin and soft tissue infection (in the previous 12 months).

Data analysis

Estimates of injecting frequency by country

To create frequency of injecting estimates among PWID by country we drew on methods used in previous reviews (Degenhardt et al., 2017). Eligible injecting frequency estimates were selected and, where multiple estimates for a country were available, pooled by country via random-effects meta-

136 analysis models in STATA using the metaprop command. To create estimates that were the most
137 temporally relevant, we included all estimates that were within 5 years of the most recent estimate. To
138 generate the estimated number of PWID based on the daily or more and less than daily estimates, we
139 multiplied the prevalence of IDU (as reported in Degenhardt et al. (2017)) by the proportion reporting
140 daily or more and less than daily injecting. The product was multiplied by the country's adult
141 population aged 15-64 years as of 2015 (UN Population Division, 2016). We estimated 95%
142 uncertainty intervals (UIs) using Monte Carlo simulation taking 100,000 draws. We used a binomial
143 distribution because our parameters of interest were proportions (the products of IDU proportion
144 among population and frequency proportions among PWID). Estimated sample sizes were derived
145 from the 95% UIs and standard errors of the proportion estimates for each country.

146 Estimates of injecting frequency by region

147 Countries were grouped according to UNAIDS, WHO and United Nations Office on Drugs and Crime
148 regions. We computed region-specific, weighted estimates of injecting frequency using all the
149 observed estimates and 95% UI of estimates in each country within that region and deriving a
150 weighted estimate and UI, based on country population size. Where regions had one (or zero) country
151 with an estimate (unless that country accounted for >50% of the region population), the global
152 estimate was imputed for the countries with evidence of IDU but without an injecting frequency
153 estimate. Otherwise, the regional estimate was imputed. We used these regional estimates to estimate
154 the global prevalence of daily or more and less than daily injecting.

155 Evaluating associations between daily or more injecting and study-level characteristics

156 We examined the study-level association between socio-demographic variables and daily or more
157 injecting and, in turn, daily or more injecting and negative health outcomes. Using meta-regression
158 analysis in STATA 15, we first built models for the 10 predictor variables and daily or more injecting
159 as the outcome variable, adjusting for region. We conducted the same analyses with daily or more
160 injecting as the predictor variable, and HIV prevalence, anti-HCV prevalence, proportion reporting
161 non-fatal overdose and skin and soft tissue infection as the independent outcome variables. We

excluded predictor variables from this analysis that were available for fewer than 25% of the total studies. Thus, self-reported engagement in OAT, stimulants as their main drug injected, recent incarceration, and skin and soft tissue infections were excluded from the analyses.

Injecting frequency and NSP coverage

To compare estimated percentages of daily or more injecting and NSP coverage by country we used Tableau 2018.2. Using country-level estimates for daily or more injecting from this study and country-level NSP coverage data (specifically, estimated number of needles and syringes distributed per PWID per year for 2015) drawn from Larney, Peacock, Leung, et al. (2017) we presented data for countries that had an estimate for both variables.

Results

Our search resulted in 61,077 sources, from which 198 studies were eligible for inclusion in this review (flowchart presented in Appendix 7). Of 179 countries with recorded evidence of injecting, there were 74 countries that had one or more estimates of injecting frequency. The studies covered data collected from 1997 to 2017; over a third of the samples were from studies that specifically recruited participants who had injected in the previous month. Recruitment criteria for recency of injecting, study and method grade, and other study-level characteristics are presented in Appendix 8.

Regional and global estimates for frequency of injecting are displayed in Table 1. Globally, we estimated that 68.1% (95% CI 64.5-71.6%) of PWID, equating to approximately 10.5 (95% UI 6.8-15.0) million people, inject daily or more frequently. Latin America (95.0%; 95%CI 93.4, 96.1%), South Asia (85.2%; 95%CI 81.8, 89.0%), and East and Southeast Asia (86.3%; 95%CI 84.6, 88.0%) had the highest estimated percentage of daily or more injecting, and Eastern Europe had the lowest percentage (41.8%; 95%CI 38.3, 45.3%).

< Table 1 here >

Figure 1 displays a map of grouped country-level estimates of daily or more injecting. Existing studies suggest that Pakistan (100.0%; 95% CI 99.7-100.0%), Colombia (99.8%; 95% CI 99.0-100.0%), Romania (99.7%; 99.2-100.0%), and Viet Nam (98.6%; 95% CI 98.0-99.1%) had the highest percentage reporting daily or more injecting, while Georgia (2.1%; 95% CI 0.8-3.4%), Taiwan (4.9%; 95% CI 2.7-8.1%) and Moldova (8.9%, 95% CI 0.8-17.1%) had the lowest. All country-level estimates are presented in Table 2. Definitions and frequency estimates by study are presented in Appendix 9.

< Figure 1 here >

< Table 2 here >

Table 3 presents the results of the univariable and multivariable meta-regression analyses with daily or more injecting as the outcome variable and socio-demographic characteristics and income-class as the explanatory variables. Greater proportion of participants reporting opioids as their main drug

injected (meta-regression coefficient [β]=0.47; 95% confidence intervals [CI] 0.23, 0.71, p<0.001) and studies from low- and middle-income class countries (β=0.03; 95%CI 0.03, 0.15, p=0.004) were associated with higher levels of daily or more injecting. Longer average duration of injecting (β=-0.02 per year; 95%CI -0.03, -0.01, p<0.001), more recent calendar period (β=-0.01 per year; 95%CI -0.02, 0.00, p=0.009), and a higher proportion of female PWID in the sample (β=-0.20; 95%CI -0.37, -0.02, p=0.032) were associated with lower levels of daily or more injecting; however, after adjusting for region there was no longer a relationship between proportion of female PWID in the sample (β=-0.05; 95%CI -0.22, 0.12, p=0.551) or income-class (β=0.03; 95%CI -0.07, 0.13), p=0.530) and daily or more injecting. There was no evidence that the proportion of the sample who were young, or who had recently experienced unstable housing were associated with level of daily or more injecting. Scatterplots displaying the results of the meta-regression analyses are presented in Appendix 10.

< Table 3 here >

< Table 4 here >

Daily or more injecting was associated with a range of study-level behaviours and health outcomes, both univariable and multivariable results are presented in Table 4. There were associations between level of daily or more injecting in the sample and proportion of the sample reporting recent receptive needle sharing (β=0.31; 95%CI 0.19, 0.43, p<0.001) and non-fatal overdose in the past 12 months (β=0.18; 95%CI 0.09, 0.27, p<0.001), and the prevalence of HIV (β=0.17; 95%CI 0.09, 0.25, p<0.001) and anti-HCV (β=0.25; 95%CI 0.12, 0.37, p<0.001) in the sample.

< Figure 2 here >

Figure 2 presents the available country-level daily or more injecting estimates with their corresponding country-level NSP coverage. There were 48 countries where both estimates were available. Country NSP coverage estimates clustered close to zero, including many of the countries reporting more frequent injecting. Figure 3 displays the same information for the top 25 countries by estimated number of PWID. The United States, China and Russia held over a third of the global IDU population injecting daily or more yet distributed less than 50 needle-syringes per PWID per year.

< Figure 3 here >

Discussion

We estimated that the majority of PWID injected daily or more (68.1%; 95% CI: 64.5-71.6%), equating to over 10 million people. In Europe, the Middle East and North Africa sampled PWID were more likely to inject less than daily. Higher levels of daily or more injecting were associated with higher prevalence of receptive needle-syringe sharing, HIV and anti-HCV prevalence, as well as higher levels of non-fatal overdose in the previous year. Notably, among countries with higher estimates of daily or more injecting, there was very low NSP coverage reported for 2015 (Larney, Peacock, Leung, et al., 2017).

There is inconsistency across studies in definitions of injecting frequency. These differences may be arbitrary, or they may be region specific, inasmuch as frequency definitions used by researchers in different countries or regions may be decided based on previously observed injecting behaviour. For example, two of the three included studies from Tehran, Iran, asked participants whether they were injecting one to three, three to six, or more than six times a day, suggestive of local knowledge of pervasive high-frequency injecting among PWID (Asli, Kandelouei, Rahimyan, Davoodbeglou, & Vaezjalali, 2016; Kandelouei et al., 2013). Frequency definitions may also differ according to research questions or aims. For instance, the Australian Illicit Drug Reporting System aimed to recruit participants with knowledge of recent drug trends. As a result, the inclusion criteria comprised at least monthly injections in the previous six months (Peacock et al., 2018). The variability of frequency of injecting variables between research studies complicates investigating and comparing injecting behaviour geographically.

To our knowledge, this is the first systematic review of frequency of injecting among PWID, which has generated estimates of global, regional and country-level frequency of injecting among PWID. There are, however, several limitations. Firstly, survey data may be inherently biased towards people who inject more frequently, and therefore is not necessarily an accurate representation of the entire PWID population. Although recruitment techniques such as respondent driven and snowball sampling are effective in reaching hidden populations, they commonly initiate recruitment from low-threshold

harm reduction services such as NSPs and drop in centres. Surveys recruiting from such services are likely to sample PWID with more frequent injecting (Brienza et al., 2000), while other service-based recruitment (e.g. drop in centres) may exclude particularly marginalised populations, or people concerned about being identified as someone who injects drugs. To reduce the risk of bias we excluded all studies that specified daily or more frequent injecting in the inclusion criteria; however, that does not eliminate inherent bias in recruitment strategies. Our results found that studies from five countries reported estimates of >98.0% for daily or more injecting, and it is difficult to determine whether the estimates are an accurate reflection of the injecting behaviour among PWID in that country or whether recruitment of participants was conducted such that people who inject more frequently were overrepresented.

Second, frequency data is typically reported categorically, and we were unable to calculate point estimates. Thus, there is limited detail to compare needle-syringe distribution coverage estimates to a more specific injecting frequency. Further, the results of this review do not reflect, and cannot discern between, regular and episodic injecting, including so-called "binge" patterns of injecting (i.e. high intensity IDU that differs from typical injecting practices). Binge injecting is independently associated with injecting risk behaviour, abscess wounds, non-fatal overdose and HIV transmission (Kerr et al., 2007; Kinner et al., 2012; Miller et al., 2006; van Beek et al., 2001; Van Hout & Bingham, 2012); however, might represent a sub-population of people who are injecting frequently.

Third, our regional and global estimates of the proportion of PWID engaging in daily or more injecting are limited by the country-level frequency data that is available. Of the 74 countries with frequency of injecting data, 47 (64%) country estimates were based on data from a single source, and 34 (46%) country estimates were based on a single estimate (compared to multiple estimates from the same source). The frequency estimates reported for Sri Lanka, Croatia, and Switzerland are presumably over-estimated (as they capture PWID who are injecting less frequently than 'daily or more') and Israel, Palestine, Afghanistan and Sweden are presumably under-estimated. We conducted a sensitivity analysis (presented in Appendix 11) excluding those seven countries and found that the confidence intervals of the estimated regional and global frequency of injecting largely overlapped

with the estimates presented in Table 1. The exception was the Middle East and North African regional estimate which, although overlapped, was much lower in the sensitivity analysis (47.3% [95%CI 42.0-52.7%] and 38.5% [95%CI 33.6-43.6%]). We would assume the three country-level estimates from this region are an underestimate of the "true" frequency estimates according to our definition. Therefore, we concluded that our presented findings are a more accurate representation of the available data.

Some regional estimates were informed by very little empirical evidence. Notably, regional estimates for the Caribbean, Latin America and Central Asia are driven by only four studies from four countries: Puerto Rico, Chile, Mexico, and Tajikistan; none of which are nationally representative. Figure 1 is a clear visualisation that highlights the need for good quality surveillance data that recruits PWID from multiple sites and covers a wider geography. National, regional and global estimates of the epidemiology of IDU and associated behaviours and characteristics are important for informing drug and harm reduction policy; however, for informative surveillance estimates to be generated there needs to be higher quality studies conducted in these missed regions where there is evidence of injecting.

While investigating the prevalence of daily or more injecting at a national level is informative, there is much sub-national variation in injecting behaviours within countries. For example, the report informing the country-level estimate for the Philippines has data from four sites, and daily or more injecting ranged from 4.0% in Zamboanga to 90.0% in Cebu (HIV and AIDS Data Hub for Asia-Pacific, 2011). The report from Azerbaijan reported similar sub-national variation, with 18.0% reporting daily or more injecting in Masalli whereas 91.0% reported daily or more injecting in Baku (Ministry of Health the Republic of Azerbaijan, 2008).

Finally, the meta-regression results may be subject to ecological fallacy, in that sample averages across studies may not be the same as the association for participants within a study (Thompson & Higgins, 2002). Relationships are more easily interpreted when there is high variation across studies compared to within studies. Therefore, the results of the meta-regression analyses should be interpreted with caution.

There may be many factors that influence the current and future frequency at which PWID are injecting. Firstly, drug market trends may limit the supply of certain drugs while increasing the availability of others. A recent example of this is the widespread cathinone injection among PWID in Hungary and Romania, and increasingly so in parts of Ireland and Scotland, resulting in binge and high frequency injection (Lafferty et al., 2016; McAuley et al., 2019; Rácz et al., 2016; Tarján et al., 2015). There is also evidence for the opposite relationship, in so much that the unavailability of certain drug types results in less frequent injecting (Day et al., 2004). Similarly, PWID in treatment, in hospital or in recovery may not be injecting as frequently or at all. The appearance of abscess wounds motivates some people to reduce their injecting to allow the wound to heal (Dunleavy, Hope, Roy, & Taylor, 2019), potentially moderating the relationship between skin and soft tissue infection and frequency of injecting. Treatment engagement may also influence injecting frequency, which has been repeatedly shown for PWID engaged in OAT. Demonstrated in a recent cohort of PWID was that those on OAT were injecting 35% less frequently than those not on OAT (Scott et al., 2015).

These findings have important implications for harm reduction services that supply needles, syringes and other injecting equipment. The WHO recently increased "high" NSP coverage from ≥200 to ≥300 needles per PWID per year (World Health Organization (WHO), 2016). Considering there is an estimated 33 needle-syringes distributed per PWID per year and 16 OAT recipients per 100 PWID globally, current coverage is clearly far from satisfactory. Further, in countries with the highest estimated percentages of daily or more injecting there was very poor or no NSP coverage. However, even in Australia, where NSP coverage is 'high' and frequency of injecting is moderate, a recent estimate determined sufficient coverage to be when 550 syringes were distributed per PWID per year (Kwon et al., 2019), almost double the WHO recommendation. Insufficient needle and syringe distribution coverage is associated with PWID reusing their own needles and sharing injecting equipment which can lead to blood borne virus transmission, bacterial infections, and vein damage (Bluthenthal, Anderson, Flynn, & Kral, 2007; O'Keefe et al., 2018; Tarján et al., 2015). Our review offers a foundation to inform more robust and country specific NSP coverage targets based on actual PWID injecting behaviour.

Our results represent a broad picture of injecting patterns among PWID globally and indicate that the majority of PWID are injecting daily or more frequently. Understanding injecting frequency is important for informing adequate NSP coverage, and we highlight the need for better surveillance data to achieve this. There is poor availability of surveillance data from many parts of the world, particularly lower socioeconomic and vulnerable populations. Finally, evidence-based harm reduction programs must be nuanced and responsive to the local drug market in order to effectively reduce the risk of harms this population is vulnerable to.

Authors' Contribution

LD, SL, MH, AP, JG, PV, ML and JL conceived the conception and design of the scope and methods of the original systematic review. SC, LD, SL and AP conceived and designed the present study. All authors made substantial contributions to the acquisition of data. SC, LD, SL, AP and JL contributed to the study methods and analysis plan. SC conducted the analysis and generated the estimates. SC produced figures. SC, LD, SL and AP contributed to the interpretation of data for the manuscript. SC drafted the first iteration of the manuscript. All authors contributed to revising the manuscript critically for important intellectual content. All authors approved the final version of the study to be published and are accountable for all aspects of the work.

Acknowledgements

The Australian National Drug and Alcohol Research Centre (NDARC), UNSW Sydney, provided funding towards the costs of this systematic review. NDARC is supported by funding from the Australian Government Department of Health under the Drug and Alcohol Program. SC acknowledges funding from PhD scholarships from the Australian National Health and Medical Research Council (NHMRC), and from the UNSW Scientia PhD Scholarship, UNSW Sydney. SL, JG, AP, and LD are supported by NHMRC Fellowships. SL and LD are supported by National Institute of Health (NIH) grants National Institute on Drug Abuse (NIDA) (R01DA1104470). JL is supported by the University of Queensland Development Fellowship. The Kirby Institute is funded by the Australian Government Department of Health and Ageing. The views expressed in this publication do not necessarily represent the position of the Australian Government. JS acknowledges funding from a PhD scholarship from the Engineering and Physical Sciences Research Council (EPSRC). EBC acknowledges funding from Canadian Network on Hepatitis C. AT has received PhD funding from the National Institute for Health Research (NIHR). MH and PV acknowledge support from NIHR Health Protection Research Unit (HPRU) in Evaluation of Interventions at University of Bristol. MH is an NIHR senior investigator and acknowledges NIHR School of Public Health Research. PV acknowledges support from the NIHR HPRU in Blood Borne and Sexually Transmitted

Infections at University College London and National Institute for Drug Abuse (grant number R01 DA037773–01A1).

Declaration of interests

In the past three years, LD has received investigator-initiated untied educational grants for studies of opioid medications in Australia from Indivior, Mundipharma, and Seqirus. SL has received investigator-initiated untied educational grants from Indivior. AP has received investigator-initiated untied educational grants from Mundipharma and Seqirus. JG is a consultant and adviser for and has received research grants from Abbvie, Cepheid, Gilead Sciences, and Merck/MSD. MH reports personal fees from Gilead, Abbvie, and MSD. JS reports non-financial support from Gilead Sciences. All other authors declare no competing interests.

Figure 1: Map of daily or more injecting by country

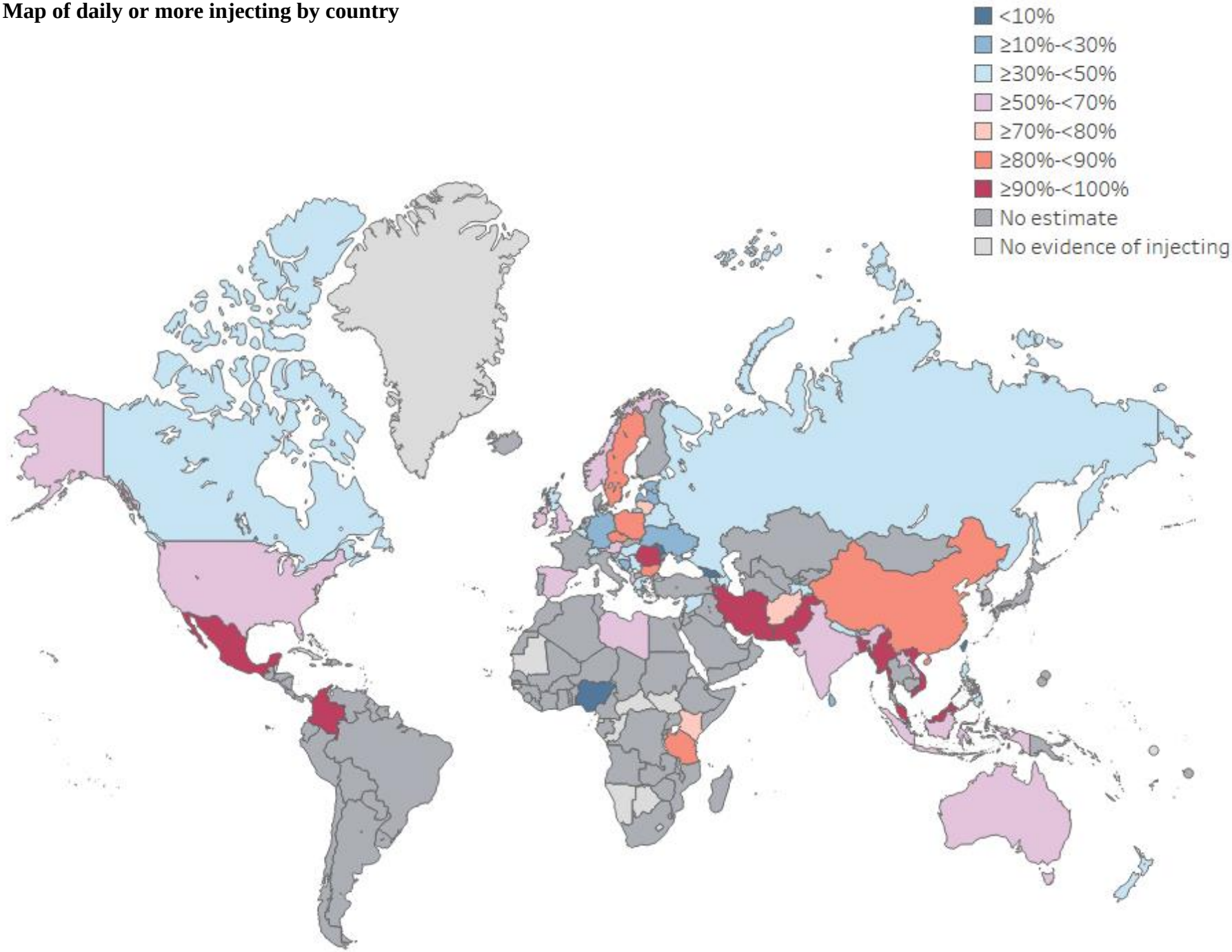
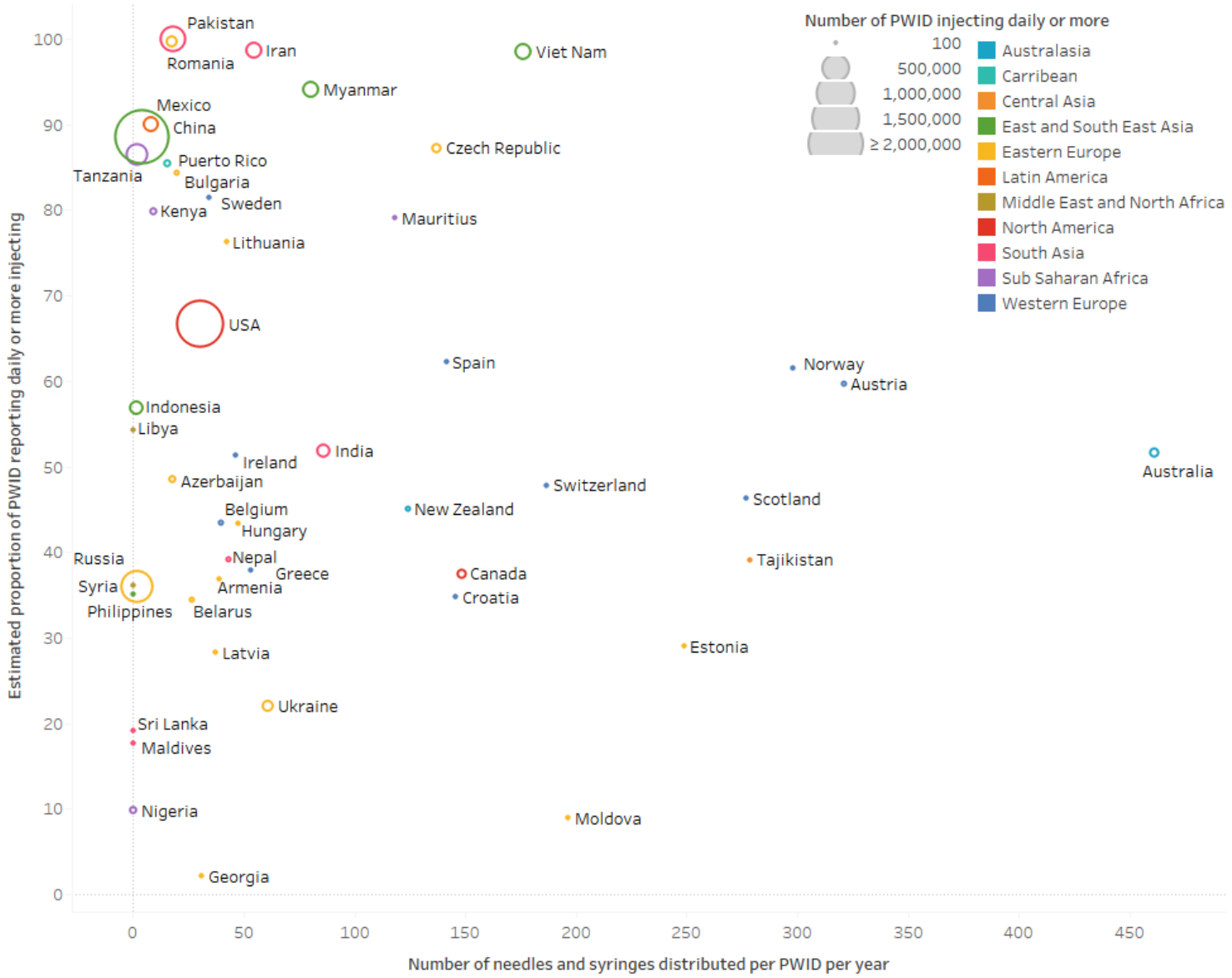
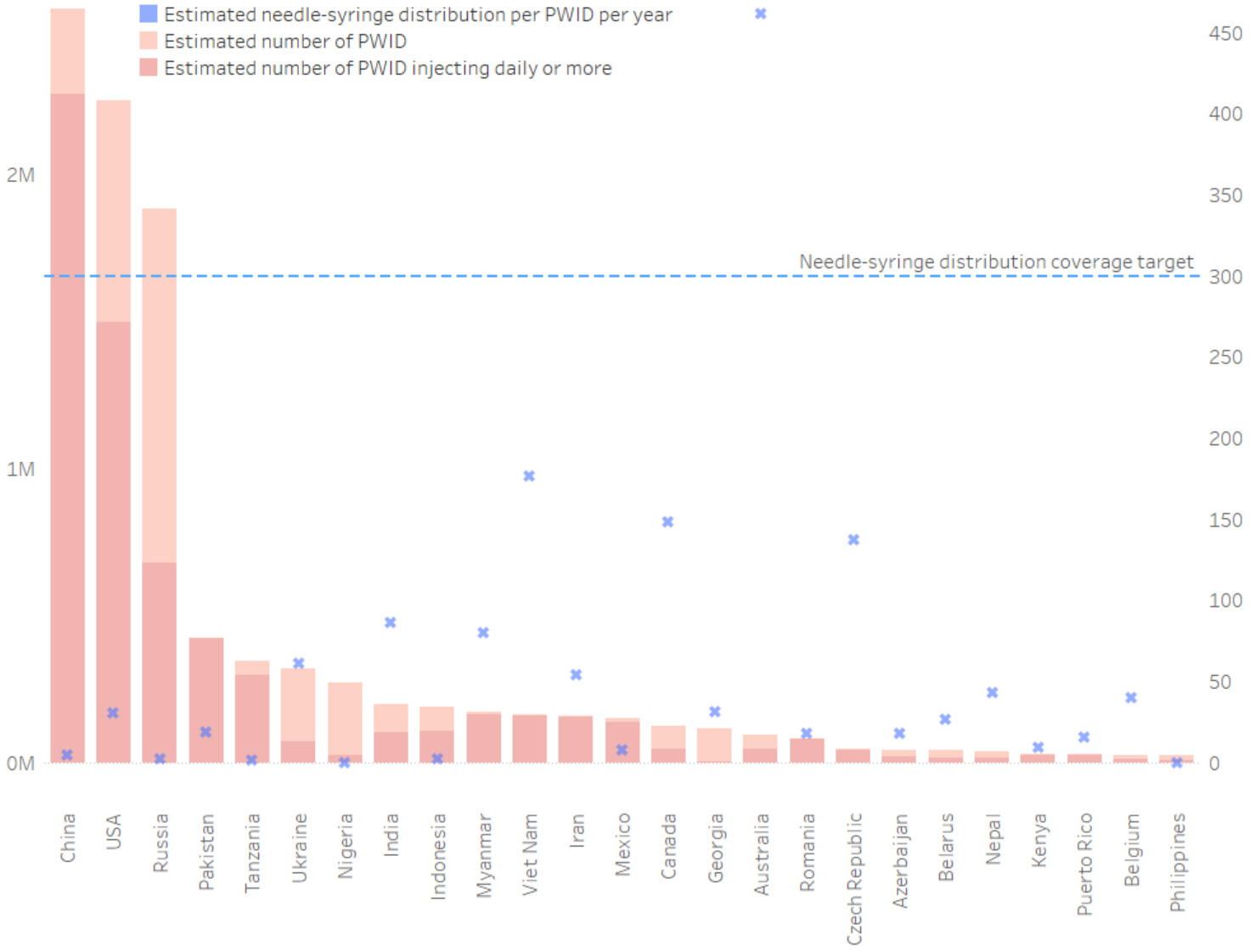


Figure 2: Daily or more injecting estimates and needle-syringe distribution coverage by country



Note: Needle-syringe distribution coverage estimates sourced from Larney, Peacock, Leung, et al. (2017).

Figure 3: Estimated number of people who are injecting daily or more and needle-syringe distribution coverage for the 25 countries with the largest number of people who inject drugs



Note: Needle-syringe distribution coverage estimates sourced from Larney, Peacock, Leung, et al. (2017).

Table 1: Frequency of injecting among people who inject drugs (PWID) by region

Region	Countries with data on frequency of injecting (n/N)	PWID injecting daily or more % (95% CI)	Number of PWID who are injecting daily or more N (95% UI)	PWID injecting less than daily % (95% CI)	Number of PWID who are injecting less than daily N (95% UI)
Eastern Europe	16/17	41.8 (38.3-45.3)	1,262,500 (647,000-1,984,000)	58.2 (54.7-61.7)	1,757,500 (817,500-2,861,000)
Western Europe	17/33	45.1 (40.8-49.5)	455,500 (321,500-622,000)	54.9 (50.5-59.2)	554,000 (361,000-784,500)
East and Southeast Asia	10/17	86.2 (84.5-88.0)	3,440,000 (2,631,500-4,296,500)	13.7 (12.0-15.4)	548,000 (410,500-702,000)
South Asia	8/9	85.2 (81.1-89.0)	871,500 (678,500-1,081,500)	14.7 (11.2-18.3)	150,000 (92,000-219,000)
Central Asia	3/5	64.0 (60.1-67.9)	180,000 (110,000-258,500)	36.0 (32.2-39.8)	101,500 (61,000-147,000)
Caribbean	1/15	73.1 (69.0-76.8)	58,000 (35,000-83,000)	26.9 (23.2-30.9)	21,500 (12,500-31,000)
Latin America	2/20	95.0 (93.4-96.1)	1,731,500 (1,276,500-2,218,000)	5.0 (4.0-6.4)	92,000 (61,000-129,000)
North America	2/2	65.1 (57.8-72.4)	1,544,500 (657,000-2,595,000)	34.9 (27.6-42.2)	827,000 (364,500-1,401,000)
Pacific Island states & terr.	0/17	NK	NK	NK	NK
Australasia	2/2	50.3 (45.0-55.6)	58,000 (41,500-76,500)	49.4 (44.2-54.6)	57,000 (40,500-75,000)
Sub-Saharan Africa	7/47	54.2 (50.3-58.0)	747,500 (262,000-1,467,000)	45.8 (42.1-49.7)	631,000 (135,500-1,358,500)
Middle East & North Africa	6/22	47.3 (42.0-52.7)	165,500 (88,000-255,000)	52.7 (47.3-58.0)	184,000 (98,000-283,500)
Global	**74/206**	68.1 (64.5-71.6)	10,529,000 (6,757,000-14,958,000)	31.9 (28.4-35.4)	4,930,500 (2,459,000-8,002,500)

Note. NK: Frequency estimates for this region are unknown

Table 2: Country-level estimates of frequency of injecting among people who inject drugs (PWID)

	Daily or more injecting		Less than daily injecting	
	Estimated percent % (CIs)	**Estimated number N (UIs)**	**Estimated percent % (CIs)**	**Estimated number N (UIs)**
Eastern Europe				
Armenia	36.9 (15.8-58.0)	5,000 (1,500-10,000)	63.1 (42.0-84.2)	8,500 (2,500-16,000)
Azerbaijan	48.5 (23.1-73.8)	21,000 (13,500-29,500)	51.5 (26.2-76.9)	22,500 (14,500-31,000)
Belarus	34.4 (19.3-49.5)	14,000 (5,000-26,500)	65.5 (50.4-80.6)	26,500 (11,000-47,000)
Bosnia & Herzegovina	20.3 (7.9-32.7)	7,000 (2,500-14,000)	79.7 (67.3-92.1)	27,500 (13,000-45,000)
Bulgaria	84.4 (81.8-86.7)	15,500 (12,500-19,000)	15.7 (13.3-18.2)	3,000 (2,000-3,500)
Czech Republic	87.2 (83.8-90.2)	41,000 (38,500-43,500)	12.8 (9.9-16.2)	6,000 (4,500-7,500)
Estonia	29.0 (20.6-37.3)	2,500 (1,000-4,500)	71.0 (62.7-79.4)	6,000 (3,000-10,000)
Georgia	2.1 (0.8-3.4)	2,500 (500-5,500)	97.8 (96.6-99.1)	112,500 (24,000-217,000)
Hungary	43.3 (39.8-46.8)	1,500 (1,000-2,500)	56.7 (53.2-60.2)	2,500 (1,000-3,500)
Latvia	28.3 (24.9-31.6)	4,000 (3,000-5,000)	71.7 (68.4-75.1)	10,000 (7,500-12,500)
Lithuania	76.3 (71.8-80.3)	3,500 (2,000-6,000)	23.8 (19.7-28.2)	1,000 (500-2,000)
Moldova	8.9 (0.8-17.1)	1,000 (<500-2,500)	91.1 (82.9-99.3)	11,000 (7,000-15,500)
Poland	84.6 (81.8-87.1)	307,000 (149,000-489,000)	15.4 (12.9-18.2)	56,000 (26,500-91,500)
Romania	99.7 (99.2-100.0)	81,000 (57,500-107,000)	0.2 (0.0-0.5)	<500 (<500-500)
Russia	36.0 (32.7-39.4)	677,000 (324,500-1,087,500)	64.0 (60.6-67.3)	1,204,000 (582,500-1,919,000)
Slovakia	NK	NK	NK	NK
Ukraine	22.0 (21.3-22.7)	70,500 (31,000-119,500)	78.0 (77.3-78.7)	249,000 (111,500-422,000)
Western Europe				
Albania	65.5 (58.5-72.1)	4,500 (3,000-6,000)	34.5 (27.9-41.5)	2,500 (1,500-3,500)
Andorra	NK	NK	NK	NK
Austria	59.7 (46.5-72.0)	11,000 (7,000-15,500)	40.3 (28.1-53.6)	7,500 (4,500-11,000)
Belgium	43.4 (36.7-50.2)	11,500 (7,000-16,000)	56.6 (49.8-63.3)	15,000 (9,500-21,000)
Croatia	34.7 (0.0-76.9)	2,000 (1,000-3,500)	65.3 (23.1-100.0)	4,000 (3,000-5,500)
Denmark	NK	NK	NK	NK
England	52.5 (51.1-54.0)	110,500 (102,500-119,000)	47.5 (46.0-48.9)	100,000 (92,500-107,500)
Finland	NK	NK	NK	NK
France	NK	NK	NK	NK
Macedonia	NK	NK	NK	NK
Germany	24.4 (20.2-28.6)	32,000 (6,500-65,000)	75.6 (71.4-79.8)	99,500 (20,500-200,000)
Greece	37.9 (36.3-39.6)	2,000 (1,500-2,500)	61.9 (60.2-63.5)	3,000 (2,500-4,000)
Iceland	NK	NK	NK	NK
Ireland	51.3 (45.6-56.9)	4,500 (3,000-5,500)	48.7 (43.1-54.4)	4,000 (3,000-5,500)
Italy	NK	NK	NK	NK
Luxembourg	NK	NK	NK	NK
Malta	NK	NK	NK	NK
Monaco	NK	NK	NK	NK
Montenegro	47.0 (43.2-50.9)	500 (500-1,000)	53.0 (49.1-56.8)	1,000 (500-1,000)
Netherlands	NK	NK	NK	NK
Northern Ireland	52.5 (51.1-54.0)	3,500 (1,500-5,500)	47.5 (46.0-48.9)	3,000 (1,500-5,000)
Norway	61.6 (59.9-63.3)	5,000 (4,500-6,000)	38.5 (36.7-40.2)	3,000 (2,500-4,000)
Portugal	NK	NK	NK	NK
San Marino	NK	NK	NK	NK
Scotland	46.3 (42.2-50.4)	7,500 (6,000-8,500)	53.7 (49.7-57.8)	8,500 (7,500-10,000)
Serbia	46.9 (42.6-51.2)	13,500 (11,000-16,500)	53.1 (48.8-57.4)	15,500 (12,500-18,500)
Slovenia	NK	NK	NK	NK
Spain	62.2 (35.3-89.2)	6,500 (2,500-11,500)	37.8 (10.8-64.7)	4,000 (1,500-7,500)
Sweden	81.5 (71.3-89.3)	6,500 (<500-26,500)	18.5 (10.8-28.7)	1,500 (<500-6,000)
Switzerland	47.9 (44.2-51.6)	6,500 (5,000-8,000)	52.2 (48.4-55.9)	7,000 (5,500-8,500)
Wales	52.5 (51.1-54.0)	5,500 (2,500-9,500)	47.5 (46.0-48.9)	5,000 (2,500-8,500)
East and South East Asia				
Brunei Darussalam	NK	NK	NK	NK

	Daily or more injecting		Less than daily injecting	
	Estimated percent % (CIs)	**Estimated number N (UIs)**	**Estimated percent % (CIs)**	**Estimated number N (UIs)**
Cambodia[a]	42.0 (33.0-51.4)	4,500 (2,000-7,500)	58.0 (48.6-67.0)	6,000 (2,500-10,500)
China	88.6 (87.3-90.0)	2,272,500 (1,753,000-2,816,000)	11.4 (10.0-12.7)	291,500 (218,500-373,000)
Indonesia	56.8 (55.4-58.3)	108,000 (89,000-128,500)	43.2 (41.7-44.6)	82,000 (67,500-97,500)
Japan	NK	NK	NK	NK
Lao	61.1 (56.9-65.2)	6,500 (5,000-8,000)	39.1 (35.0-43.3)	4,000 (3,000-5,500)
Malaysia	91.1 (89.2-93.0)	256,500 (213,500-302,000)	8.9 (7.0-10.8)	25,000 (18,500-32,500)
Mongolia	NK	NK	NK	NK
Myanmar	94.1 (91.8-96.3)	163,000 (110,000-222,000)	6.0 (3.7-8.2)	10,500 (5,500-16,500)
Philippines	35.1 (0.0-74.1)	9,000 (5,000-14,000)	65.1 (26.3-100.0)	16,500 (11,500-22,500)
South Korea	NK	NK	NK	NK
Singapore	NK	NK	NK	NK
Taiwan	4.9 (2.7-8.1)	2,000 (1,000-3,500)	95.1 (92.0-97.3)	43,500 (33,000-54,000)
Thailand[a]	59.8 (55.4-64.2)	31,000 (11,500-54,000)	40.2 (35.8-44.6)	20,500 (7,500-36,500)
Timor L'Este	NK	NK	NK	NK
Viet Nam	98.6 (98.0-99.1)	158,500 (121,500-198,000)	0.8 (0.4-1.1)	1,000 (500-2,000)
South Asia				
Afghanistan	78.8 (65.8-91.8)	109,500 (68,500-156,500)	21.1 (8.0-34.1)	29,500 (11,500-53,000)
Bangladesh	96.8 (95.7-97.6)	66,500 (61,500-71,500)	3.3 (2.4-4.3)	2,000 (1,500-3,000)
Bhutan	NK	NK	NK	NK
India	51.9 (46.9-57.0)	102,500 (66,500-142,000)	47.8 (44.1-51.5)	94,500 (62,000-130,000)
Iran	98.7 (96.9-100.0)	156,000 (108,500-208,000)	0.6 (0.0-1.9)	1,000 (<500-3,000)
Maldives	17.6 (13.2-22.1)	500 (-500)	82.4 (77.9-86.8)	1,000 (500-2,000)
Nepal	39.1 (15.4-62.8)	14,000 (8,500-19,000)	60.9 (37.2-84.6)	21,500 (16,000-27,000)
Pakistan	100.0 (99.7-100.0)	422,500 (364,000-483,500)	0.0 (0.0-0.2)	<500 (<500-500)
Sri Lanka	19.1 (15.0-23.9)	<500 (<500-<500)	80.9 (76.2-85.0)	500 (500-500)
Central Asia				
Kazakhstan[a]	79.9 (76.2-83.3)	90,000 (55,000-128,500)	20.1 (16.7-23.9)	22,500 (13,500-33,500)
Kyrgyzstan[a]	76.7 (72.9-80.3)	22,000 (13,500-31,500)	23.3 (19.7-27.1)	6,500 (4,000-9,500)
Tajikistan	39.1 (34.8-43.6)	9,000 (5,500-13,500)	60.9 (56.4-65.2)	14,500 (8,500-20,500)
Turkmenistan	NK	NK	NK	NK
Uzbekistan	NK	NK	NK	NK
Caribbean				
Bahamas	NK	NK	NK	NK
Bermuda	NK	NK	NK	NK
Puerto Rico	85.4 (81.0-89.1)	24,000 (14,500-34,500)	14.6 (10.9-19.0)	4,000 (2,500-6,500)
Dominican Republic	NK	NK	NK	NK
Haiti	NK	NK	NK	NK
Jamaica	NK	NK	NK	NK
Latin America				
Argentina	NK	NK	NK	NK
Bolivia	NK	NK	NK	NK
Brazil	NK	NK	NK	NK
Chile	NK	NK	NK	NK
Colombia	99.8 (99.0-100.0)	153,000 (112,000-196,500)	0.1 (0.0-0.4)	<500 (<500-500)
Costa Rica	NK	NK	NK	NK
Ecuador	NK	NK	NK	NK
El Salvador	NK	NK	NK	NK
Guatemala	NK	NK	NK	NK
Guyana	NK	NK	NK	NK
Honduras	NK	NK	NK	NK
Mexico	90.1 (87.7-92.1)	136,000 (88,500-187,000)	10.1 (8.0-12.5)	15,000 (9,500-22,000)
Nicaragua	NK	NK	NK	NK
Panama	NK	NK	NK	NK
Paraguay	NK	NK	NK	NK
Peru	NK	NK	NK	NK
Suriname	NK	NK	NK	NK

	Daily or more injecting		Less than daily injecting	
	Estimated percent % (CIs)	**Estimated number N (UIs)**	**Estimated percent % (CIs)**	**Estimated number N (UIs)**
Uruguay	NK	NK	NK	NK
Venezuela	NK	NK	NK	NK
North America				
Canada	37.5 (30.6-44.4)	46,000 (34,500-59,000)	62.5 (55.6-69.4)	77,000 (61,000-94,500)
United States	66.6 (59.3-74.0)	1,498,500 (622,000-2,536,000)	33.4 (26.0-40.7)	750,000 (303,500-1,306,500)
Pacific Island States & Territories				
American Samoa	NK	NK	NK	NK
Federated States of Micronesia	NK	NK	NK	NK
Fiji	NK	NK	NK	NK
French Polynesia	NK	NK	NK	NK
Guam	NK	NK	NK	NK
Kiribati	NK	NK	NK	NK
Marshall Islands	NK	NK	NK	NK
New Caledonia	NK	NK	NK	NK
Northern Mariana Islands	NK	NK	NK	NK
Palau	NK	NK	NK	NK
Papua New Guinea	NK	NK	NK	NK
Samoa	NK	NK	NK	NK
Solomon Islands	NK	NK	NK	NK
Tonga	NK	NK	NK	NK
Vanuatu	NK	NK	NK	NK
Australasia				
Australia	51.6 (45.9-57.3)	48,000 (35,000-62,500)	48.1 (42.5-53.6)	44,500 (32,500-58,500)
New Zealand	45.0 (41.3-48.7)	10,000 (7,000-13,500)	55.0 (51.3-58.7)	12,500 (8,500-16,500)
Sub Saharan Africa				
Angola	NK	NK	NK	NK
Benin[a]	22.9 (18.8-27.5)	4,000 (1,000-7,500)	77.1 (72.6-81.2)	13,000 (2,500-25,500)
Burkina Faso	NK	NK	NK	NK
Burundi	NK	NK	NK	NK
Cameroon	NK	NK	NK	NK
Cape Verde	NK	NK	NK	NK
Chad	NK	NK	NK	NK
Cote d'Ivoire	NK	NK	NK	NK
Democratic Republic of Congo	NK	NK	NK	NK
Djibouti	NK	NK	NK	NK
Ethiopia	NK	NK	NK	NK
Gabon	NK	NK	NK	NK
Gambia	NK	NK	NK	NK
Ghana	NK	NK	NK	NK
Guinea	NK	NK	NK	NK
Kenya	79.9 (74.5-84.5)	24,500 (9,500-43,000)	20.2 (15.5-25.5)	6,000 (2,000-11,500)
Liberia	NK	NK	NK	NK
Madagascar[a]	4.2 (0.0-8.8)	500 (<500-3,500)	95.8 (91.2-100.0)	15,000 (<500-67,500)
Malawi	NK	NK	NK	NK
Mali	NK	NK	NK	NK
Mauritius	79.0 (76.5-81.5)	5,500 (1,500-10,000)	21.0 (18.5-23.5)	1,500 (500-2,500)
Mozambique	NK	NK	NK	NK
Niger	NK	NK	NK	NK
Nigeria	9.8 (4.7-14.9)	26,500 (5,000-60,000)	90.2 (85.1-95.2)	244,000 (49,500-485,000)
Rwanda	NK	NK	NK	NK
Senegal	NK	NK	NK	NK

	Daily or more injecting		Less than daily injecting	
	Estimated percent % (CIs)	**Estimated number N (UIs)**	**Estimated percent % (CIs)**	**Estimated number N (UIs)**
Seychelles[a]	46.5 (41.2-51.9)	500 (500-1,000)	53.5 (48.1-58.8)	1,000 (500-1,000)
Sierra Leone	NK	NK	NK	NK
Somalia	NK	NK	NK	NK
South Africa	NK	NK	NK	NK
Swaziland	NK	NK	NK	NK
Togo	NK	NK	NK	NK
Uganda	NK	NK	NK	NK
Tanzania	86.5 (83.5-89.1)	296,500 (178,500-426,000)	13.6 (11.0-16.5)	46,500 (26,500-70,000)
Zambia	NK	NK	NK	NK
Zimbabwe	NK	NK	NK	NK
Middle East and North Africa				
Algeria	NK	NK	NK	NK
Bahrain	NK	NK	NK	NK
Cyprus	NK	NK	NK	NK
Egypt	NK	NK	NK	NK
Iraq	NK	NK	NK	NK
Israel	65.3 (58.3-71.9)	4,000 (2,000-6,000)	34.7 (28.1-41.7)	2,000 (1,000-3,000)
Jordan	NK	NK	NK	NK
Kuwait	NK	NK	NK	NK
Lebanon[a]	51.9 (40.5-63.1)	2,500 (1,500-4,000)	48.2 (36.9-59.5)	2,500 (1,000-3,500)
Libya	54.3 (48.7-59.8)	1,000 (500-1,500)	45.7 (40.3-51.3)	1,000 (500-1,500)
Morocco[a]	91.5 (86.9-94.9)	28,000 (14,500-42,500)	8.5 (5.1-13.1)	2,500 (1,000-4,500)
Palestine	55.6 (51.3-60.0)	2,000 (1,000-2,500)	44.4 (40.0-48.7)	1,500 (500-2,000)
Oman	NK	NK	NK	NK
Qatar	NK	NK	NK	NK
Saudi Arabia	NK	NK	NK	NK
Sudan	NK	NK	NK	NK
Syria	36.1 (31.3-41.1)	4,500 (2,500-7,000)	63.9 (58.9-68.7)	8,500 (4,500-12,500)
Tunisia	NK	NK	NK	NK
Turkey	NK	NK	NK	NK
United Arab Emirates	NK	NK	NK	NK
Yemen	NK	NK	NK	NK

Note. [a] The estimates for injecting frequency deviated from our definition by 3 injections and were therefore excluded from estimating the regional prevalence of frequency. The definitions can be found in Appendix 8.
NK: There is evidence of injecting in this country but there were no estimates of injecting frequency available.
For the following countries there is no reported evidence of injecting: (Western Europe) Greenland and Liechtenstein; (East and Southeast Asia) North Korea; (Caribbean) Antigua and Barbuda, Barbados, Cuba, Dominica, Grenada, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Trinidad and Tobago; (Latin America) Belize; (Pacific Island States and Territories) Nauru and Tuvalu; (Sub Saharan Africa) Botswana, Central African Republic, Comoros, Equatorial Guinea, Eritrea, Guinea Bissau, Lesotho, Mauritania, Namibia, Republic of the Congo and Sao Tome and Principe; (Middle East and North Africa) South Sudan.

Table 3: Univariable and multivariable study-level exposure variables associated with daily or more injecting among people who inject drugs

Study-level exposure variables	N	Univariable models				Multivariable models[e]			
		β[a]	SE[b]	95% CIs	*p*	β	SE	95% CIs	*p*
Proportion of the sample who are female	**269**	**-0.20**	**0.09**	**(-0.37, -0.02)**	**0.032**	-0.05	0.09	(-0.22,0.12)	0.551
Proportion of the sample reporting opioids as main drug injected	**104**	**0.47**	**0.12**	**(0.23, 0.71)**	**<0.001**	**0.36**	**0.13**	**(0.10,0.62)**	**0.007**
Year of data collection	**329**	**-0.01**	**0.00**	**(-0.02, 0.00)**	**0.009**	**-0.01**	**0.00**	**(-0.02,0.00)**	**0.033**
Proportion of the sample reporting unstable housing/homelessness[c]	111	0.21	0.12	(-0.03, 0.46)	0.085	0.19	0.12	(-0.04,0.43)	0.097
Proportion of the sample who are young[d]	201	0.12	0.10	(-0.08, 0.32)	0.229	-0.09	0.09	(-0.27,0.10)	0.370
Duration of injecting of the sample	**169**	**-0.02**	**0.00**	**(-0.03, -0.01)**	**<0.001**	**-0.01**	**0.00**	**(-0.02,0.00)**	**0.025**
Income level[f] (vs. High-income)									
Low- and middle-income class	**329**	**0.09**	**0.03**	**(0.03, 0.15)**	**0.004**	0.03	0.05	(-0.07,0.13)	0.530

Note. [a] Meta-regression coefficient
[b] Standard error
[c] In the previous 12 months
[d] Aged <25 years
[e] Adjusted for region
[f] Country-level income class

Table 4: Study-level outcome variables associated with daily or more injecting among people who inject drugs

Study-level outcome variables	N	Univariable models				Multivariable models[e]			
		β[a]	SE[b]	95% CIs	*p*	β	SE	95% CIs	*p*
Injecting risk behaviour[c]	**124**	**0.31**	**0.06**	**(0.19, 0.43)**	**<0.001**	**0.34**	**0.06**	**(0.21, 0.47)**	**<0.001**
HIV prevalence	**218**	**0.17**	**0.04**	**(0.09, 0.25)**	**<0.001**	**0.18**	**0.04**	**(0.09, 0.27)**	**<0.001**
Anti-HCV prevalence	**173**	**0.25**	**0.06**	**(0.12, 0.37)**	**<0.001**	**0.38**	**0.07**	**(0.25, 0.50)**	**<0.001**
Non-fatal overdose[d]	**36**	**0.18**	**0.04**	**(0.09, 0.27)**	**<0.001**	**0.24**	**0.06**	**(0.13, 0.36)**	**<0.001**

Note. [a] Meta-regression coefficient
[b] Standard error
[c] Self-report receptive sharing of needles and/or syringes in the previous month
[d] Self-reported non-fatal overdose within the previous 12 months
[e] Adjusted for region

References

Asli, M., Kandelouei, T., Rahimyan, K., Davoodbeglou, F., & Vaezjalali, M. (2016). Characterization of occult hepatitis B infection among injecting drug users in Tehran, Iran. *Hepatitis Monthly, 16 (3) (no pagination)*(e34763). doi:http://dx.doi.org/10.5812/hepatmon.34763

Blackburn, N. A., Lancaster, K. E., Ha, T. V., Latkin, C. A., Miller, W. C., Frangakis, C., . . . Go, V. F. (2017). Characteristics of persons who inject drugs and who witness opioid overdoses in Vietnam: A cross-sectional analysis to inform future overdose prevention programs. *Harm Reduction Journal, 14*(1), 62. doi:http://dx.doi.org/10.1186/s12954-017-0188-4

Bluthenthal, R. N., Anderson, R., Flynn, N. M., & Kral, A. H. (2007). Higher syringe coverage is associated with lower odds of HIV risk and does not increase unsafe syringe disposal among syringe exchange program clients. *Drug and Alcohol Dependence, 89*(2), 214-222. doi:https://doi.org/10.1016/j.drugalcdep.2006.12.035

Brienza, R. S., Stein, M. D., Chen, M.-H., Gogineni, A., Sobota, M., Maksad, J., . . . Clarke, J. (2000). Depression among needle exchange program and methadone maintenance clients. *Journal of Substance Abuse Treatment, 18*(4), 331-337. doi:https://doi.org/10.1016/S0740-5472(99)00084-7

Brugal, M. T., Barrio, G., De La Fuente, L., Regidor, E., Royuela, L., & Suelves, J. M. (2002). Factors associated with non-fatal heroin overdose: assessing the effect of frequency and route of heroin administration. *Addiction, 97*, 319-327.

Corneil, T. A., Kuyper, L. M., Shoveller, J., Hogg, R. S., Li, K., Spittal, P. M., . . . Wood, E. (2006). Unstable housing, associated risk behaviour, and increased risk for HIV infection among injection drug users. *Health & Place, 12*(1), 79-85. doi:https://doi.org/10.1016/j.healthplace.2004.10.004

Darke, S., Swift, W., Hall, W., & Ross, M. (1994). Predictors of injecting and injecting risk-taking behaviour among methadone maintenance clients. *Addiction, 89*, 311-316.

Day, C., Degenhardt, L., Gilmour, S., & Hall, W. (2004). Effects of reduction in heroin supply on injecting drug use: analysis of data from needle and syringe programmes. *BMJ, 329*(7463), 428-429. doi:10.1136/bmj.38201.410255.55

Degenhardt, L., Peacock, A., Colledge, S., Leung, J., Grebely, J., Vickerman, P., . . . Larney, S. (2017). Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. *The Lancet Global Health, 5*(12), e1192-e1207. doi:10.1016/s2214-109x(17)30375-3

Dunleavy, K., Hope, V., Roy, K., & Taylor, A. (2019). The experiences of people who inject drugs of skin and soft tissue infections and harm reduction: A qualitative study. *International Journal of Drug Policy, 65*, 65-72. doi:https://doi.org/10.1016/j.drugpo.2018.09.001

HIV and AIDS Data Hub for Asia-Pacific. (2011). IHBSS Philippines.

Kandelouei, T., Hosseini, S. M., Gachkar, L., Keyvani, H., Davoodbeglou, F., & Vaezjalali, M. (2013). Reduction in prevalence of hepatitis B surface antigen among intravenous drug users in Tehran drop-in-centers. *Archives of Clinical Infectious Diseases, 8 (2) (no pagination)*(e15531).

Kerr, T., Fairbairn, N., Tyndall, M., Marsh, D., Li, K., Montaner, J., & Wood, E. (2007). Predictors of non-fatal overdose among a cohort of polysubstance-using injection drug users. *Drug Alcohol Depend, 87*(1), 39-45. doi:10.1016/j.drugalcdep.2006.07.009

Kinner, S. A., Milloy, M. J., Wood, E., Qi, J., Zhang, R., & Kerr, T. (2012). Incidence and risk factors for non-fatal overdose among a cohort of recently incarcerated illicit drug users. *Addict Behav, 37*(6), 691-696. doi:10.1016/j.addbeh.2012.01.019

Korsmeyer, P., & Kranzler, H. R. (2009). Encyclopedia of drugs, alcohol & addictive behavior.

Kwon, J. A., Iversen, J., Law, M., Dolan, K., Wand, H., & Maher, L. (2019). Estimating the number of people who inject drugs and syringe coverage in Australia, 2005–2016. *Drug and Alcohol Dependence, 197*, 108-114. doi:https://doi.org/10.1016/j.drugalcdep.2018.11.033

Lafferty, C., Smith, L., Coull, A., & Shanley, J. (2016). The experience of an increase in the injection of ethylphenidate in Lothian April 2014–March 2015. *Scottish Medical Journal, 61*(2), 74-83. doi:10.1177/0036933016649871

Larney, S., Peacock, A., Leung, J., Colledge, S., Hickman, M., Vickerman, P., . . . Degenhardt, L. (2017). Global, regional, and country-level coverage of interventions to prevent and manage HIV and hepatitis C among people who inject drugs: a systematic review. *The Lancet Global Health, 5*(12), e1208-e1220. doi:10.1016/s2214-109x(17)30373-x

Larney, S., Peacock, A., Mathers, B. M., Hickman, M., & Degenhardt, L. (2017). A systematic review of injecting-related injury and disease among people who inject drugs. *Drug Alcohol Depend, 171*, 39-49. doi:10.1016/j.drugalcdep.2016.11.029

MacArthur, G. J., Minozzi, S., Martin, N., Vickerman, P., Deren, S., Degenhardt, L., & Hickman, M. (2012). Opiate substitution treatment and HIV transmission in people who inject drugs: a systematic review and meta-analysis. *BMJ, 345*. doi:10.1136/bmj.e5945

Mattick, R. P., Breen, C., Kimber, J., & Davoli, M. (2009). Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *Cochrane Database Syst Rev*(3), CD002209. doi:10.1002/14651858.CD002209.pub2

McAuley, A., Yeung, A., Taylor, A., Hutchinson, S. J., Goldberg, D. J., & Munro, A. (2019). Emergence of Novel Psychoactive Substance injecting associated with rapid rise in the population prevalence of hepatitis C virus. *International Journal of Drug Policy, 66*, 30-37. doi:https://doi.org/10.1016/j.drugpo.2019.01.008

Miller, C. L., Kerr, T., Frankish, J. C., Spittal, P. M., Li, K., Schechter, M. T., & Wood, E. (2006). Binge Drug Use Independently Predicts HIV Seroconversion Among Injection Drug Users: Implications for Public Health Strategies. *Substance Use & Misuse, 41*(2), 199-210. doi:10.1080/10826080500391795

Ministry of Health the Republic of Azerbaijan. (2008). Prevalence of HIV, Hepatitis and Syphilis, and Behavioural Risk Factors Among Most-At-Risk Groups in the Republic of Azerbaijan.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & The, P. G. (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLOS Medicine, 6*(7), e1000097. doi:10.1371/journal.pmed.1000097

National Institute on Drug Abuse. (2007). The Neurobiology of Drug Addiction. Retrieved from https://www.drugabuse.gov

Noroozi, M., Armoon, B., Ghisvand, H., Noroozi, A., Karimy, M., Bazrafshan, M. R., . . . Dieji, B. (2018). Prevalence and risk factors for injection site skin infections among people who inject drugs (PWID) in Tehran. *J Cosmet Dermatol*. doi:10.1111/jocd.12675

O'Keefe, D., Aung, S. M., Pasricha, N., Wun, T., Linn, S. K., Lin, N., . . . Dietze, P. (2018). Measuring individual-level needle and syringe coverage among people who inject drugs in Myanmar. *International Journal of Drug Policy, 58*, 22-30. doi:https://doi.org/10.1016/j.drugpo.2018.04.010

Peacock, A., Gibbs, D., Sutherland, R., Uporova, J., Karlsson, A., Bruno, R., . . . Farrell, M. (2018). *Key Findings from the National Illicit Drug Reporting System (IDRS) Interviews*. Retrieved from Sydney:

Platt, L., Minozzi, S., Reed, J., Vickerman, P., Hagan, H., French, C., . . . Hickman, M. (2018). Needle and syringe programmes and opioid substitution therapy for preventing HCV transmission among people who inject drugs: findings from a Cochrane Review and meta-analysis. *Addiction, 113*(3), 545-563. doi:10.1111/add.14012

Rácz, J., Csák, R., Tóth, K. T., Tóth, E., Rozmán, K., & Gyarmathy, V. A. (2016). Veni, vidi, vici: The appearance and dominance of new psychoactive substances among new participants at the largest needle exchange program in Hungary between 2006 and 2014. *Drug and Alcohol Dependence, 158*, 154-158. doi:https://doi.org/10.1016/j.drugalcdep.2015.10.034

Rafful, C., Wagner, K. D., Werb, D., González-Zúñiga, P. E., Verdugo, S., Rangel, G., & Strathdee, S. A. (2015). Prevalence and correlates of neck injection among people who inject drugs in Tijuana, Mexico. *Drug and Alcohol Review, 34*(6), 630-636. doi:10.1111/dar.12264

Robinson, W. T., Kazbour, C., Nassau, T., Fisher, K., Sheu, S., Rivera, A. V., . . . Brady, K. (2017). Brief Report: Nonfatal Overdose Events Among Persons Who Inject Drugs: Findings From Seven National HIV Behavioral Surveillance Cities 2009 & 2012. *Journal of acquired immune deficiency syndromes (1999), 75 Suppl 3*, S341-S345. doi:https://dx.doi.org/10.1097/QAI.0000000000001426

Schoenbaum, E. E., Hartel, D., Selwyn, P. A., Klein, R. S., Davenny, K., Rogers, M., . . . Friedland, G. (1989). Risk factors for human immunodeficiency virus infection in intravenous drug users. *The New England Journal of Medicine, 321*(13), 874-879.

Scott, N., Caulkins, J., Ritter, A., & Dietze, P. (2015). *How patterns of injecting drug use evolve in a cohort of people who inject drugs.* Retrieved from Canberra: Australian Institute of Criminology: https://aic.gov.au/publications/tandi/tandi502

Stevens, G. A., Alkema, L., Black, R. E., Boerma, J. T., Collins, G. S., Ezzati, M., . . . Welch, V. (2016). Guidelines for Accurate and Transparent Health Estimates Reporting: the GATHER statement. *The Lancet, 388*(10062), e19-e23. doi:https://doi.org/10.1016/S0140-6736(16)30388-9

Tarján, A., Dudás, M., Gyarmathy, V. A., Rusvai, E., Tresó, B., & Csohán, Á. (2015). Emerging Risks Due to New Injecting Patterns in Hungary During Austerity Times. *Substance Use & Misuse, 50*(7), 848-858. doi:10.3109/10826084.2015.978672

Thompson, S. G., & Higgins, J. P. T. (2002). How should meta-regression analyses be undertaken and interpreted? *Statistics in Medicine, 21*, 1559-1573. doi:10.1002/sim.1187

Todd, C. S., Nasir, A., Stanekzai, M. R., Fiekert, K., Rasuli, M. Z., Vlahov, D., & Strathdee, S. A. (2011). Prevalence and correlates of HIV, syphilis, and hepatitis B and C infection and harm reduction program use among male injecting drug users in Kabul, Afghanistan: A cross-sectional assessment. *Harm Reduction Journal, 8*(1), 22. doi:10.1186/1477-7517-8-22

UN Population Division. (2016). *World population prospects: the 2015 revision*. Retrieved from New York: https://esa.un.org/unpd/wpp/Publications/Files/Key_Findings_WPP_2015.pdf

van Beek, R., Dwyer, A., & Malcol, I. (2001). Cocaine injecting: the sharp end of drug-related harm! *Drug and Alcohol Review, 20*(3), 333-342. doi:10.1080/09595230120079657

Van Hout, M. C., & Bingham, T. (2012). "A Costly Turn On": Patterns of use and perceived consequences of mephedrone based head shop products amongst Irish injectors. *International Journal of Drug Policy, 23*(3), 188-197. doi:https://doi.org/10.1016/j.drugpo.2012.01.008

Wilson, H., Brener, L., Mao, L., & Treloar, C. (2014). Perceived discrimination and injecting risk among people who inject drugs attending Needle and Syringe Programmes in Sydney, Australia. *Drug and Alcohol Dependence, 144*, 274-278. doi:https://doi.org/10.1016/j.drugalcdep.2014.08.018

World Bank. (2018). World Bank list of economies (June 2018). from The World Bank Group https://databank.worldbank.org/data/home.aspx

World Health Organization (WHO). (2016). *Global Health Sector Strategy on Viral Hepatitis 2016-2021: Towards Ending Viral Hepatitis*. Retrieved from Geneva, Swizterland: